

A REVIEW ON VARIANT OF CONCERN (DELTA VARIANT OF COVID 19)***Kanchan K. Jangam, Dattaprasad. N. Vikhe, Ravindra S. Jadhav and Ganesh S. Shinde**

Department of Pharmacognosy, Pravara Rural College of Pharmacy, Pravaranagar Maharashtra, India 413736.

***Corresponding Author: K. K. Jangam**

Department of Pharmacognosy, Pravara Rural College of Pharmacy, Pravaranagar Maharashtra, India 413736.

Article Received on 10/09/2021

Article Revised on 30/09/2021

Article Accepted on 20/10/2021

ABSTRACT

The B.1.617.2 Delta variant of the severe acute respiratory syndrome coronavirus (SARS –COV-2). The virus that causes coronavirus disease 2019 (COVID-19), has contributed to a surge in cases of Republic of India and has currently been detected across the world, as well as a notable increase in cases within the UK. Delta and (B.167.2.1)/(Ay.1) could be a new variant of the SARS- CoV-2. coronavirus came in existence because of a mutation within the delta strain of the virus (B.1.617.2 variant). It is technically successive generation of SARS-COV-2. This mutant of delta was initially detected in Europe in March 2021. The delta virus that was initially detected in Republic of India (in February 2021) eventually became an enormous downside for the total world. However, the delta variant at the moment, is restricted to smaller areas within the country. Individual's reportable symptoms like headaches, sore throats, fluid noses, and fever. The World Health Organization (WHO) is following this variant as a part of the delta variant as well as for different variants of concern with extra mutations. This review provides detail idea about delta virus its treatment, prevention and methods for reduction of sensitivity.

KEYWORDS: Delta variant, Spike Proteins, antibody neutralization, Delta plus variant, Vaccines.**INTRODUCTION**

The B.1.617 that is SARS-CoV-2 linkage ended up being identified in 2020 in Asia in October. This has then come to be dominant in some Indian areas, British and distribute this is certainly more many countries. The lineage includes three subtypes being main B.1.617.1, B.1.617.2 and B.1.617.3, harboring diverse Spike mutations in the domain that is n-terminal) together with receptor binding domain (RBD) which may increase their resistant evasion potential. B.1.617.2, also termed Delta that is variant considered to spread quicker than many other alternatives. Right here, isolated a Delta that is infectious strain a traveler returning from Asia, examined its sensitivity to monoclonal antibodies (mAbs) and to antibodies contained in sera from COVID-19 convalescent people or vaccine recipients, when compared to other viral strains.

The Delta that is variant has been detected in many nations. It's become prevalent in the condition of Maharashtra and most likely various other regions. It that is Indian been classified as a Variant of Concern (VOC) and it is thought to be 60% more transmissible than variant Alpha. Little is well known about its sensitivity into the humoral reaction that is protected. Recent reports indicated a sensitivity this is certainly paid down of associated with B.1.617 lineage to particular monoclonal and antibodies which are polyclonal.^[1-8] Extreme respiratory this is certainly acute coronavirus 2 (SARS-

CoV-2), the causative broker of coronavirus disease (COVID-19), has encountered transformative evolution since its emergence when you look at the human population in 2019. On 31 May 2021, Health company has actually designated four variations of SARS-CoV-2 as variants of concern (VOC)— Alpha, Beta, Gamma, and Delta corresponding to the Assignment that is phylogenetic of international Outbreak (Pango) lineage designation B.1.1.7, B.1.351, P.1 and B.1.617.2, correspondingly.

Multiple SARS-CoV-2 variants are circulating in Japan and because of the large transmissibility of the VOC, the replacement of locally circulating strains by Alpha and Delta VOC poses a general public that is serious menace in Japan. Right here we used a design that is renewal-equation-based describe the adaptive advancement among multiple variations, i.e., R.1, Alpha and Delta alternatives as well as ordinary variation, in the country to inform risk-assessment.^[9]

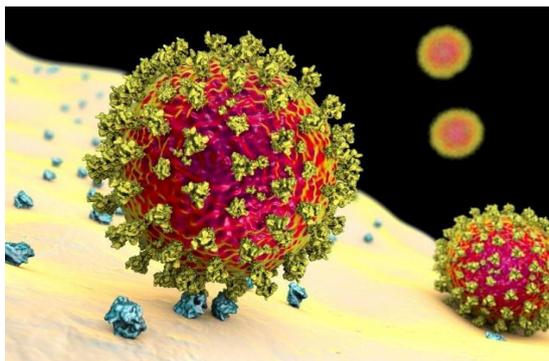


Fig. 1: Spike Protein Receptor Binding.

Augmentation of Delta Variant

Pretty much all new cases of covid-19 are the delta variant but data which can be new that while instance numbers are increasing, “Cases are increasing rapidly around the world and the delta variant is now prominent. The rise is primarily in more youthful age ranges, a percentage that is huge of were unvaccinated but are today being asked to receive the vaccine. It is motivating to see that medical center admissions and deaths are not increasing at the rate that is exact same but we’ll continue steadily to monitor it closely.” the info showed there clearly was a higher danger of hospital entry for clients aided by the delta variation compared with the alpha variation, but its analysis uncovered that two amounts of vaccine provided a qualification this is certainly a lot of against medical center entry, believed is a lot more than 90%. The newest data show 99% of sequenced and genotyped instances around the world are the delta^[10-13] this is certainly variant.

Afflicted Population

Over 12 months in to the coronavirus condition (COVID-19) pandemic, new alternatives continue steadily to emerge and spread quickly over the continents.^[14] The Delta this is certainly SARS-CoV-2 variant initially identified in Asia, was initially detected in London Care domiciles are disproportionately affected by the pandemic, with high fatality rates reported among older people.^[15,16] Care home residents and staff had been, consequently, prioritized for vaccination as quickly once the first vaccines that are COVID-19 readily available.

The assault this is certainly saturated in this care residence outbreak, especially among partially vaccinated residents, is consistent with reduced security against SARS-CoV-2 infection in residents and staff who’d obtained only one dosage.

“The limited data circulated from PHE demonstrably indicates that outbreaks regarding the delta variant in schools exceed those who work in some other environment this is certainly defined that instances among secondary school children are the greatest across all age ranges, and rising rapidly.” Latest information through the working office for National Statistics show

that variety of instances of covid-19 have been rising fastest in schoolchildren in years 7 to 11.^[17]

Safeguard for Delta Variant

Medical trial data suggest that a dosage this is certainly solitary of Comirnaty (BNT162b2 mRNA, BioNTech-Pfizer, Mainz, Germany/New York, united states of America (US)) vaccine ended up being predicted to deliver 89% protection from symptomatic disease.^[18] in contrast to 95% for just two amounts provided 3 weeks aside.^[19] Considering these early clinical trial data suggesting fast protection after having a single dosage regarding the Comirnaty vaccine, the UK (UK) opted for an extended interval all the way to 12 days involving the two-dose routine for COVID-19 vaccines to speed up the rollout associated with very first dosage associated with the vaccine to those at risk.^[20] that is highest.

Moreover, clinical tests aided by the Vaxzevria vaccine demonstrated a far better boost with longer intervals between vaccine amounts.^[21] Real-world data have shown effectiveness that is large particularly in stopping hospitalizations and deaths – by way of a solitary dose of either vaccine, despite having the greater transmissible Alpha (B.1.1.7) variant,^[22,23] or in high risk settings such as care homes Countries which have opted to extend the interval between two vaccine amounts should consider offering the dosage this is certainly 2nd to care home residents and staff, into the framework associated with the circulating Delta variant.^[24]

Recent Advancement

A. Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization

The cross-reactivity of monoclonal Abs to pre-existing SARS-CoV-2 strains, sera from long-lasting convalescent people and vaccine this is certainly present against an infectious Delta isolate. Some mAbs, including Bamlanivimab, destroyed binding to your Spike and no longer neutralized variant Delta. Further program that Delta is less responsive to sera from naturally immunized individuals. Vaccination of convalescent individuals boosted the humoral reaction this is certainly protected above the threshold of neutralization. These outcomes highly claim that vaccination of previously contaminated people is most protective that is likely a sizable variety of circulating viral strains, including variant Delta. An individual dosage of either Pfizer or AstraZeneca vaccines barely caused neutralizing antibodies against variant Delta in people that are not formerly contaminated with SARS-CoV-2.

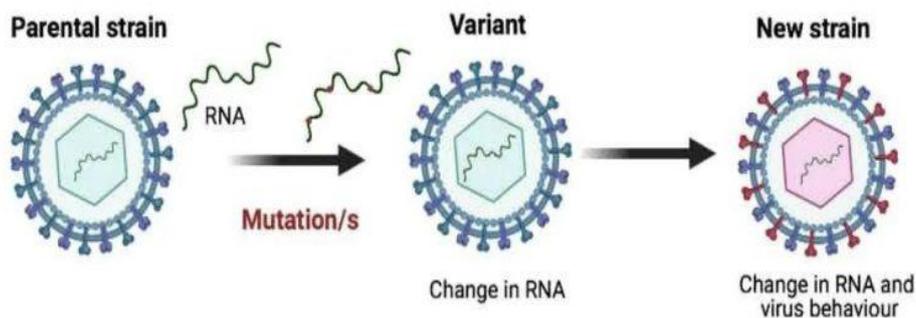


Fig. 2: Journey strains to new strains via variant.

Neutralizing antibody levels are very predictive of protected defense against symptomatic illness,^[25] This is certainly SARS-CoV-2. A study this is certainly present all sequenced symptomatic instances of COVID-19 in England had been used to calculate the influence of vaccination on disease. Effectiveness was notably lower with Delta than with Alpha after one dosage of AstraZeneca or Pfizer vaccines. The effectiveness that is two-dose Delta ended up being calculated to be 60% and 88% for AstraZeneca and Pfizer vaccines, correspondingly.^[26] Neutralization experiments indicate that Pfizer and AstraZeneca antibodies that are vaccine-elicited efficacious against variant Delta, but about 3-5-fold less potent than against variant Alpha.

There clearly was no difference that is major the levels of antibodies elicited by Pfizer or AstraZeneca vaccines. Potential limitations of our work come with a reduced range vaccine recipients examined plus the not enough characterization of mobile immunity, which may be much more cross-reactive compared to the response this is certainly humoral. Future work with increased individuals and longer study periods helps define the role of humoral answers in vaccine effectiveness against circulating variations. Outcomes demonstrate that the growing variant Delta partially but dramatically escapes neutralizing mAbs, and polyclonal antibodies elicited by earlier illness that is SARS-CoV-2 vaccination.

B. Neutralizing capability against Delta (B.1.617.2) and other alternatives of concern Comirnaty that is following (BioNTech/Pfizer)

Readily available information declares that vaccination with Comirnaty is effective up against the Alpha, Beta and Gamma VOCs, albeit at different degrees.^[27-29] The presence of mutations such as for example L452R and P681R into the increase this is certainly SARS-CoV-2 receptor binding domain of this Delta variant, proved to be associated with large transmissibility,^[30] besides the fast spread and surge of severe situations of the variant when you look at the Indian sub-continent in present months, raised concern about the impact with this variant and its particular ability to evade SARS-CoV-2 vaccines,^[31] Demonstrate right here that neutralizing levels against both Delta isolates had been somewhat paid down, although just by two parts weighed against the herpes virus this is certainly initial. Undoubtedly,

research that is recent showed that the Delta VOC is paid down by 2.5 folds when compared with a Wuhan-related SARS-CoV-2 strain in individuals 4 to 2 weeks following a second dose of Comirnaty.^[32] While merely a reduction that is 1.7-fold noticed when it comes to Alpha VOC compared to the first virus, our results show a 10-fold reduction in neutralizing titers contrary to the Beta VOC as well as 2 fold decrease resistant to the Gamma VOC. Undoubtedly, a research this is certainly recent that neutralizing titers against both the Beta and Gamma VOCs are reduced by eight to 12-fold and fourfold, respectively.^[33,34,35] Interestingly, effectiveness associated with Comirnaty vaccine ended up being recently shown to be 75% against any reported infection with all the Beta variant and 97.4% against serious, critical, or disease.^[36] this is certainly deadly. This information declare that Comirnaty vaccination is most likely, safety against the Delta VOC since lowering of neutralizing levels from the Delta ended up being significantly less than the beta variation. The data provided here contribute to the growing evidence of effectiveness regarding the mRNA-based Comirnaty vaccine against understood VOCs and highlight the importance of vaccination particularly in places with high percentage of VOC blood supply skills of this research would be the utilization of wild type isolated viruses and not mutated pseudo-viruses to gauge the full reaction that is neutralizing evaluating neutralization of two different and phylogenetically distinct Delta isolates.

Limitations associated with the research range from the number this is certainly small of analysed, the powerful over representation of females (31 of 36 participants) and also the not enough T-cell reaction evaluation. In this scholarly study we assessed the neutralizing capacity of sera from the HCW. That is vaccinated against Delta and never Kappa VOC. The Kappa VOC also started in India where it was circulating since October 2020, albeit Delta could be the dominant circulating that is sub-lineage. General results declare that despite somewhat neutralization that is reduced, Comirnaty vaccination induces an amazing antibody reaction also when it comes to Delta VOC. Additional researches are essential to verify the vaccine effectiveness in wider populace groups. Decreased neutralization of SARS-CoV-2 B.1.617 by vaccine and serum that is convalescent acute breathing syndrome coronavirus 2 (SARS-CoV-2) has

encountered modern modification, with alternatives conferring benefit quickly getting prominent lineages, e.g., B.1.617. With evident increased transmissibility, variant B.1.617.2 has contributed to the present revolution of infection ravaging the Indian subcontinent and has already been designated a variation of concern in Britain.

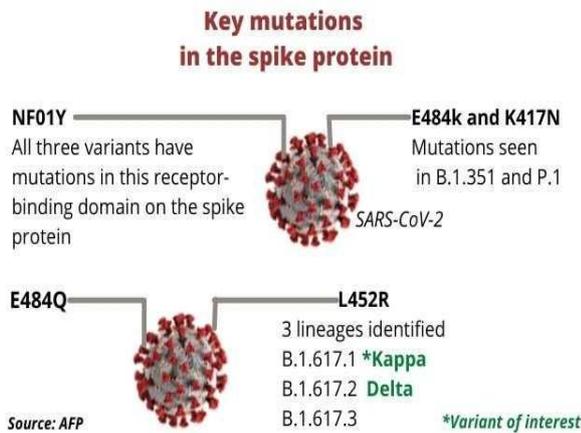


Fig. 3: Key mutation in the spike proteins.

The capability of organism antibodies and convalescent and immunizing agent sera to neutralize B.1.617.1 and B.1.617.2, complement this with structural analyses of Fab/receptor binding domain (RBD) complexes, and map the world this is often definitely substance of variations. Neutralization of each viruses is paid off in distinction to ancestral strains that area unit Wuhan-related however there's but no proof of intensive protein escape as seen with B.1.351. However, B.1.351 and P.1 sera showed markedly even a lot of reduction in neutralization of B.1.617.2, suggesting that people contaminated antecedently by these variants could also be a lot of susceptible to reinfection by B.1.617.2. This observance provides vital ideas which may be current protection arrange with future variant vaccines in non-immune communities.

Delta to dominate world

“Globally there is heaps of concern with respect to the delta variant, beside World successfulness Organization is troubled concerning this collectively. Presently, delta is recorded as a result of the second most variant that is dominant of worldwide. The variation can also be dispersing quickly through Europe at around eighty thousand instances detected up to presently.

It is phoning for the speed of EU vaccination programs, noting that a dose that is twin nearly constant protection against the delta variant as against older of us. The rest associated with international globe suffering delta. Lockdowns being enforced in higher city, Australian Continent, following significantly over 100 spic-and-span cases of the variation. Israel has actually reintroduced a mandate on face masks alone 10 times once lifting it, following foreign instances of delta.

However, to be peer assessed, discovered delta not merely spreads rather a lot of merely than earlier alternatives, but evades immunizing agent defense higher. even so, whereas immunizing agent effectiveness had been paid down the conclusions show that it's notwithstanding protective against extreme illness.^[37]

India's hassle of data and morbidity

Asia believed the wrath associated with pandemic throughout the ordinal trend that is COVID-19. although several instant sociopolitical aspects, that were express by the Editors. But cause that is chronic India's issues: the knowledge crisis. With the exception of the many efforts being state led Asia still does not have the official, in public offered, nationwide, high-resolution (at town or village degree) medical science and successfulness capability data assortment on COVID-19. Such data would possibly want helped to ascertain the crisis that is prospective of provide and totally different sources, in turn averting fatalities.

India's successfulness data a definite merchandise that is scarce with constant battles over fine quality. although straightforward to know, this irritating downside needs grappling through aggressive assets at intervals the gathering and management of top-quality data on health effects and ways. The hurdles to data that are clear square measure disclosed into the continuing pandemic a combine of which they are pervasive on the so much facet pandemic-related data resources, like data from the Pradhan Mantri Arogya Yojana and successfulness management and concepts System. Offered data bear inconvenience and insufficiency. The Ministry of Health and Family Welfare has utilized its Twitter handle to supply intermittent state level COVID-19 data in hobbies year. even so, state level aggregates are short for developing the analytical ideas needed for native tips which can be targeted. As Associate in Nursinging example, subnational data from the age and intercourse composition of COVID-19 incidence and death is elusive, obstructing study to know World Health Organization is prone or anticipate needs. Closely associated with insufficiency is that the format that is inaccessible that data are generally provided. as an example, the Association for Socially Applicable studies have dedicated sources being substantial herb and collate data from footage, PDFs, and various totally different obscure platforms for pandemic analysis. the shortage of freely gettable and knowledge being merely accessible COVID-19 vaccination center geolocations has prevented the Association for Socially Applicable analysis.^[38]

Delta Plus Variant

The variant this can be definitely new of i.e. B.1.617.2 has really arrived, that has been 1st seen in India and additionally this delta variation is slowly being found in numerous alternative nations additionally.

Many people square measure terribly aggravated owing

to the delta variant, owing to which individuals that square measure several in addition lost their life. so as to avoid this, the nationwide government is turning out with an oversized quantity of efforts and vaccination has in addition been created no-cost, therefore everybody may probably get a vaccination. The delta variation has been discovered once the second wave of covid-19, though the wave this can be definitely second not entirely over but. owing to no matter changes attended within the sort of coronavirus, for the rationale that of this that the delta variation is formed, which can be in addition spreading quickly.

The delta variant is dispersing quickly, its things have additionally detected in geographic region, Madhya Pradesh, Tamil Nadu, geographical area. Why do not we tend to tell you that the key section of corona virus is critical supermolecule this can be definitely spike as a result of that it spreads infection by visiting the body.

Earlier, Associate in Nursing alpha variation of covid finished up being seen that unfold quickly among our body, but the delta variant spreads the unhealthiness within our body hr. faster than this, that's additionally changing into thought-about dangerous. people square measure very frightened thanks to the delta variant as a result of getting the immunogen doesn't eliminate the corona virus, instead it lowers the modifications, however this variation that's new of has seen scores of rates altogether folks.

Delta Plus Variant Symptoms

Numerous symptoms of delta variation were seen, about which we are going to provide total information and you ought to know about its signs, because then you will be in a position to effortlessly discover whether you have delta variant or no if you have total information. In this variation, you will probably find signs like dry coughing, tiredness, or temperature overall. Extreme symptoms of this variant can include difficulty breathing or discomfort this is certainly abdominal. You will find may various other outward indications of the delta variant, such as for example skin rash, improvement in along with of this throat, shortness of breath, in addition to loss of odor, diarrhea, hassle, or nose that is runny etc.

Common signs and symptoms of the delta variation are considered. Then go ahead and get the vaccination done as quickly as possible and take drugs depending on the guidance for the medical practioners if you see some of this sign. Hope the severity is understood by you for this delta variation and get yourself addressed in the first if you notice any outward symptoms

Delta Plus Variant Cause

Because of the delta variation, there has become a large amount of stir one of the individuals and everyone is very annoyed with this specific brand-new variant of covid 19. the reason that is just this scatter with this virus is an infection because this virus is spread selectively or

shut to each other and switches into the body through respiration etc.

And because of its primary part protein that is spike. It is dispersing rapidly truly in our human body. Up to now, no obvious information has-been obtained about where this virus originated from and just how it began then we are able to additionally undergo this virus if we walk out the house and satisfy men and women or touch any object that might content herpes.

Delta plus Variant Safety Measures

To prevent the delta virus, you have to take care of some special things, about which we're going to give you information this is certainly complete. Kindly read the real things given below very carefully, that are the following

- Try not to venture out of this homely residence without important work.
- Maintain a distance of 6 foot while fulfilling individuals.
- Work with a sanitizer whenever anyone who is meeting.
- Sanitize and items that are disinfect things found in your house.
- Wash the hands with detergent for 20 sec times that are a few times.
- Then make use of a double mask when you have to go out of the home for many important works.
- Just use after disinfecting and washing almost everything extracted from outdoors.
- The essential thing that is essential to get the vaccination done as soon as possible to avoid this.

Delta Plus Variant Treatment

B.1.617.2 primarily health practitioners utilized antibiotics for the treatment but no information that is obvious been gotten about this. The way in which is just prevent this is getting vaccinated as soon as possible. so far, plenty of vaccines being granted for covid-19 all around the globe and a quantity this is certainly large of have already got this vaccine as well as a many folks are getting this vaccine every day.

It has been said that no treatment is working against this variant and it is perhaps not entirely expunged even because of the vaccine, however the odds of getting unwell from this through vaccination is very less.

Things to be recall

It's determined from delta plus variant that does not walk out the homely home without having any explanation.

Make use of mask, and a sanitizer and would go to your covid facilities which can be closest and gets your vaccination done.

The us government is making many attempts in order to avoid this condition, however you'll avoid this disease if yourself are vigilant about it.

If you notice any observable symptoms for this, don't be careless and consult medical practitioners as soon as possible and in India to vaccines which are numerous come for this like – Pfizer, covishield, covaxin, sputnik, etc.^[39]

CONCLUSION

Delta is more infectious compared to other virus strains. Unvaccinated folks are in danger. Vaccination could be the security that is best against delta, which Reduced susceptibility of SARS-CoV-2 variant Delta to antibody neutralization. Delta labeled as a variant of concern by the union ministry of family and wellness welfare [MOHFW], individuals have been cautioned against it. Generally, there is must be alert about signs, triggers safety measures and treatment.

REFERENCE

1. Yadav, P. D. *et al.* Neutralization of variant under investigation B.1.617 with sera of BBV152 vaccinees. *Clinical Infectious Diseases*, <https://doi.org/10.1093/cid/ciab411>, 2021.
2. Ferreira, I. *et al.* SARS-CoV-2 B.1.617 emergence and sensitivity to vaccine-elicited antibodies. *Biorxiv*, 2021.2005.2008.443253, <https://doi.org/10.1101/2021.05.08.443253>, 2021.
3. Hoffmann, M. *et al.* SARS-CoV-2 variant B.1.617 is resistant to Bamlanivimab and evades antibodies induced by infection and vaccination. *Biorxiv*, 2021.2005.2004.442663, <https://doi.org/10.1101/2021.05.04.442663>, 2021.
4. Cherian, S. *et al.* Convergent evolution of SARS-CoV-2 spike mutations, L452R, E484Q and P681R, in the second wave of COVID-19 in Maharashtra, India. *Biorxiv*, 2021.2004.2022.440932, <https://doi.org/10.1101/2021.04.22.440932>, 2021.
5. Edara, V.-V. *et al.* Infection and vaccine-induced neutralizing antibody responses to the SARS-CoV-2 B.1.617.1 variant. *Biorxiv*, 2021.2005.2009.443299, <https://doi.org/10.1101/2021.05.09.443299>, 2021.
6. Tada, T. *et al.* The Spike Proteins of SARS-CoV-2 B.1.617 and B.1.618 Variants Identified in India Provide Partial Resistance to Vaccine-elicited and Therapeutic Monoclonal Antibodies. *Biorxiv*, 2021.2005.2014.444076, <https://doi.org/10.1101/2021.05.14.444076>, 2021.
7. Liu, J. *et al.* BNT162b2-elicited neutralization of B.1.617 and other SARS-CoV-2 variants. *Nature*, <https://doi.org/10.1038/s41586-021-03693-y>, 2021.
8. Wall, E. C. *et al.* Neutralising antibody activity against SARS-CoV-2 VOCs B.1.617.2 and B.1.351 by BNT162b2 vaccination. *The Lancet* 397, 2331-2333, [https://doi.org/10.1016/S0140-6736\(21\)01290-3](https://doi.org/10.1016/S0140-6736(21)01290-3), 2021.
9. World Health Organization (WHO). SARS-CoV-2 Variants of Concern and Variants of Interest. Geneva: WHO; 2021. Available from: <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/>.
9. Public Health England. Variants: distribution of case data, 11 June 2021. 18June2021. www.gov.uk/government/publications/covid-19-variants-genomically-confirmed-case-numbers/variants-distribution-of-case-data-18-june-2021.
10. Public Health England. Effectiveness of covid-19 vaccines against hospital admission with the Delta (B.1.617.2) variant, 14 June 2021. https://khub.net/web/phe-national/public-library/-/document_library/v2Ws-RK3ZIEig/view/479607266.
11. Public Health England. Investigation of SARS-CoV-2 variants of concern: technical briefings. 18 June 2021. www.gov.uk/government/publications/investigation-of-novel-sars-cov-2-variant-variant-of-concern-20201201.
12. Independent SAGE. The Independent Sage Report 44: Continuing need for support measures. 18 June 2021. www.independentsage.org/wp-content/uploads/2021/06/Supprt-document-final.pdf.
13. The Public Health England (PHE) Variant Technical Group. SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 10. London: PHE. [Accessed: 15 Jun 2021]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/984274/Variants_of_Concern_VOC_Technical_Briefing_10_England.pdf
14. Patel MC, Chaisson LH, Borgetti S, Burdsall D, Chugh RK, Hoff CR, et al. Asymptomatic SARS-CoV-2 infection and COVID-19 mortality during an outbreak investigation in a skilled nursing facility. *Clin Infect Dis.*, 2020; 71(11): 2920-6. <https://doi.org/10.1093/cid/ciaa763> PMID: 32548628.
15. McMichael TM, Currie DW, Clark S, Pogojans S, Kay M, Schwartz NG, et al. Epidemiology of Covid-19 in a longterm care facility in King County, Washington. *N Engl J Med*, 2020; 382(21): 2005-11.
16. Office for National Statistics. Coronavirus (covid-19) infection survey, UK. 4 Jun 2021. <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/coronaviruscovid19infectionsurvey/pilot/4june2021#age-analysis-of-the-number-of-people-who-had-covid-19>.
17. United States Food and Drug Administration (FDA). Pfizer- BioNTech COVID-19 vaccine emergency use authorization review memorandum. Silver Spring: FDA; 2020. Available from: <https://www.fda.gov/media/144416/download>
18. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 Mrna Covid-19 vaccine. *N Engl J Med*, 2020; 383(27): 2603-15. <https://doi.org/10.1056/NEJMoa2034577> PMID: 33301246

19. Public Health England (PHE). COVID-19: the green book, chapter 14a. London, PHE. [Accessed: 11 Jun 2021]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/984310/Greenbook_chapter_14a_7May2021.pdf.
20. Voysey M, Costa Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. *Lancet*, 2021; 397(10277): 881-91. [https://doi.org/10.1016/S0140-6736\(21\)00432-3](https://doi.org/10.1016/S0140-6736(21)00432-3) PMID: 33617777.
21. Lopez Bernal J, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. *BMJ.*, 2021; 373(1088): n1088. <https://doi.org/10.1136/bmj.n1088> PMID: 33985964.
22. Vasileiou ESC, Simpson CR, Robertson C, Shi T, Kerr S, Agrawal U, et al. Effectiveness of First Dose of COVID-19 Vaccines Against Hospital Admissions in Scotland: National Prospective Cohort Study of 5.4 Million People, 2021. <https://doi.org/DOI:10.2139/ssrn.3789264>.
23. Shrotri M, Krutikov M, Palmer T, Giddings R, Azmi B, Subbarao S, et al. Vaccine effectiveness of the first dose of ChAdOx1nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of Long-Term Care Facilities (VIVALDI study). *medRxiv*. 2021.03.26.21254391. <https://doi.org/10.1101/2021.03.26.21254391>.
24. Houry, D. S. *et al.* Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nature Medicine*, <https://doi.org/10.1038/s41591-021-01377-8>, 2021.
25. Bernal, J. L. *et al.* Effectiveness of COVID-19 vaccines against the B.1.617.2 variant. *medRxiv*, 2021.2005.2022.21257658, <https://doi.org/10.1101/2021.05.22.21257658>, 2021.
26. Lustig Y, Nemet I, Kliker L, Zuckerman N, Yishai R, Alroy-Preis S, et al. Neutralizing Response against Variants after SARSCoV-2 Infection and One Dose of BNT162b2. *N Engl J Med.*, 2021; 384(25): 2453-4. <https://doi.org/10.1056/NEJMc2104036> PMID: 33826815.
27. Wang P, Casner RG, Nair MS, Wang M, Yu J, Cerutti G, et al. Increased resistance of SARS-CoV-2 variant P.1 to antibody neutralization. *Cell Host Microbe*, 2021 May 12; 29(5): 747-51 e4.
28. Liu Y, Liu J, Xia H, Zhang X, Zou J, Fontes-Garfias CR, et al. BNT162b2-Elicited Neutralization against New SARS-CoV-2 Spike Variants. *N Engl J Med*, 2021. NEJMc2106083. <https://doi.org/10.1056/NEJMc2106083> PMID: 33979486.
29. Cherian S, Potdar V, Jadhav S, Yadav P, Gupta N, Das M, et al. Panda S Convergent evolution of SARS-CoV-2 spike mutations, L452R, E484Q and P681R, in the second wave of COVID-19 in Maharashtra, India. *BioRxiv*, 2021. <https://doi.org/10.1101/2021.04.22.440932>
30. Callaway E. Delta coronavirus variant: scientists brace for impact. *Nature*, 2021 Jun 22. <https://doi.org/http://dx.doi.org/10.1038/d41586-021-01696-3> . PMID: 34158664.
31. Liu C, Ginn HM, Dejnirattisai W, Supasa P, Wang B, Tuekprakhon A, et al. Reduced neutralization of SARS-CoV-2 B.1.617 by vaccine and convalescent serum. *Cell*, 2021. Available from: <https://www.cell.com/action/showPdf?pii=S0092-8674%2821%2900755-8>.
32. Wang P, Casner RG, Nair MS, Wang M, Yu J, Cerutti G, et al. resistance of SARS-CoV-2 variant P.1 to antibody neutralization. *Cell Host Microbe*, 2021 May 12; 29(5): 747-51 e4.
33. Shen X, Tang H, Pajon R, Smith G, Glenn GM, Shi W, et al. Neutralization of SARS-CoV-2 Variants B.1.429 and B.1.351. *N Engl J Med*, 2021; 384(24): 2352-4. <https://doi.org/10.1056/NEJMc2103740> PMID: 33826819
34. Virtanen J, Uusitalo R, Korhonen EM, Aaltonen K, Smura T, Kuivanen S, et al. Kinetics of Neutralizing Antibodies of COVID-19 Patients Tested Using Clinical D614G, B.1.1.7, and B.1.351 Isolates in Microneutralization Assays. *Viruses*, 2021; 13(6): 996. <https://doi.org/10.3390/v13060996> PMID:34073577
35. Abu-Raddad LJ, Chemaitelly H, Butt AA, National Study Group for COVID-19 Vaccination. Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants. *N Engl J Med*, 2021. NEJMc2104974. <https://doi.org/10.1056/NEJMc2104974> PMID: 33951357
36. Daily coronavirus news round-up Online every weekday at 6pm BST newscientist.com/coronavirus-latest
37. www.thelancet.com Vol 397 June 26, 2021
38. <https://www.mpnrc.org/delta-plus-variant-symptoms-cause-precaution-treatment/>